PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 72.2)

To:

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JAPON

Date of mailing *(day/month/year)* 30 September 2004 (30.09.2004)	
Applicant's or agent's file reference M3-A0201P	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2003/002918	International filing date *(day/month/year)* 12 March 2003 (12.03.2003)
Applicant JAPAN SCIENCE AND TECHNOLOGY CORPORATION et al	

1. **Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. **Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, CO, EP, GH, KG, KR, MK, MZ, RO, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, BA, BB, BG, BR, BY, BZ, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PH, PL, PT, SC, SD, SE, SG, SK, SL, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 90 90

Form PCT/IB/338 (July 1996)

Translation

PCT/JP2003/002918

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M3-A0201P	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/002918	International filing date (*day/month/year*) 12 March 2003 (12.03.2003)	Priority date (*day/month/year*) 12 March 2002 (12.03.2002)
International Patent Classification (IPC) or national classification and IPC C12N 15/12, C07K 14/47, 16/18, C12Q 1/48, C12P 21/02, G01N 33/50, 33/15, 33/53, A61K 45/00, 38/00, 39/395, A61P 35/00, 43/00		
Applicant JAPAN SCIENCE AND TECHNOLOGY CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29 August 2003 (29.08.2003)	08 January 2004 (08.01.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/002918

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP03/02918

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 10, 12-14

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 10, 12-14.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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PCT/JP03/02918

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-6, 8-9, 11	YES
	Claims	7	NO
Inventive step (IS)	Claims		YES
	Claims	1-9, 11	NO
Industrial applicability (IA)	Claims	1-9, 11	YES
	Claims		NO

2. Citations and explanations

Document 1: JP, 60-185719, A (Ajinomoto Co., Inc.), 21 September, 1985 (21.09.85)
Document 2: Jpn. J. Pharmacol., 1993, 63 (2), pages 195-202
Document 3: J. Biol. Chem., 2001, 276 (46), pages 42744-42752
Document 4: J. Cell. Sci., 1994, 107 (Pt1), pages 253-265
Document 5: Genes Cells, 1996, 1 (11), pages 977-993
Document 6: J. Biol. Chem. 1996, 271 (7), pages 3779-3786
Document 7: J. Biol. Chem. 1994, 269 (49), pages 31034-31040
Document 8: JP, 2001-161398, A (Medical & Biological Laboratories Co., Ltd.), 19 June, 2001 (19.06.01)
Document 9: EP, 118665, A1 (Medical & Biological Laboratories Co., Ltd.), 6 March, 2002 (06.03.02)
Document 10: WO, 01-11367, A1 (Medical & Biological Laboratories Co., Ltd.), 15 February, 2001 (15.02.01)
Document 11: Anal. Biochem., February 2002, 301 (1), pages 65-74

The subject matter of claim 7 does not appear to be novel or to involve an inventive step in view of documents 1 and 2 cited in the ISR.

Document 1 describes staurosporine that has a strong effect of inhibiting the growth of cells derived from humans.

Document 2 describes the compound, K-252a, that inhibits the proliferation of smooth muscle cells derived from bovines.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The subject matter of claim 7 relates to a cell-proliferation inhibitor that contains a compound defined by a desired property, i.e., being "selected by a screening method of claim 6," as an active ingredient. The subject matter of claim 7 encompasses the cell-proliferation inhibitors that contain any of the compounds of such property, as an active ingredient; however, only a small part of the compounds claimed therein are disclosed as meant in PCT Article 5, and it is not supported by the disclosure in the specification in the sense of PCT Article 6.

For the "cell-proliferation inhibitors that contain compounds selected by the screening method of claim 6, as an active ingredient," it is impossible to define the scope of compounds having such property, even in view of the common technical knowledge at the time of the filing, and so the subject matter of claim 7 does not satisfy the requirement of clarity of PCT Article 6.

This International Preliminary Examination is therefore carried out only on the cell-proliferation inhibitors containing as an effective ingredient the compounds that are concretely described as being selected by means of the screening method of claim 6 (i.e., lowering the level of phosphorylation by the kinase activity of a Cdc7/ASK complex).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : V

The subject matters of claims 1-9 and 11 do not appear to involve an inventive step in view of documents 3-11 cited in the ISR.

Document 3 describes that an amino acid residue to be phosphorylated by a Cdc7/ASK complex is contained in the first to sixty-second places of the N-terminus of mouse MCM2 and that the kinase activity of Cdc7/ASK complex is essential to the DNA replication of eukaryotes.

Document 4 describes the amino acid sequence of BM28 (human homologue of MCM2).

Document 5 describes the amino acid sequence of mouse MCM2.

Documents 6 and 7 describe a method wherein (1) a protein phosphorylated by a protein kinase is trypsinized, (2) the peptide fragment that contains the amino acids to be phosphorylated by the said protein kinase is identified by means of ^{32}P used as a label, and then (3) the said fragment is analyzed by means of the Edman degradation, whereby the said amino acids to be phosphorylated are identified, and so such method was a well-known technology at the priority time claimed in the present application.

Documents 8-11 describe (a) methods for measuring the activity of a protein kinase by means of an antibody to recognize the state of amino acid phosphorylation in a protein to be phosphorylated, and (b) screening methods for compounds that inhibit or promote the protein-phosphorylation activity of the said protein kinase on the said protein to be phosphorylated, and so such methods of both (a) and (b) were well-known technologies at the priority time claimed in the present application.

Accordingly, a person skilled in the art could have easily (1) identified the amino acids to be phosphorylated by a Cdc7/ASK complex in MCM2 described in documents 3-5, prepared an antibody to recognize the state of phosphorylation of the said amino acids, and measured the kinase activity of the Cdc7/ASK complex by means of the said antibody; (2) screened compounds that inhibit or promote the kinase activity of a Cdc7/ASK complex by such measurement; and (3) used compounds obtained by means of such screening for cell-proliferation inhibitors.